Influenza Like Illness: 18 months Surveillance at Pokhara Academy of Health Sciences

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ABSTRACT

Introduction: Several viruses can cause clinical features similar to influenza. The term 'influenza-like illness' is used to describe the clinical features that can be attributed to infection caused by influenza and other respiratory viruses. Influenza infection can result in mild to serious illness,with significant mortality rates worldwide. Pokhara Academy of Health Sciences, Western Regional Hospital, Pokhara is one of the sentinel sites for human surveillance of influenza in Nepal that is maintained by Walter Reed/ AFRIMS Research Unit Nepal (WARUN). The objective of this study is to analyze demographic and laboratory parameters of cases of influenza like illness.

Materials and Methods: A retrospective study was conducted from July 1st 2018– December 31st 2019 at Pokhara Academy of Health Sciences, Pokhara. Approval for research was obtained from National Health Research Council, Kathmandu. Demographic features were noted, temperature was measured in each case and reports of influenza tests were recorded. Results: 1213 subjects were enrolled during study period and 63% were males. Most patients were in age group <15 years (82.5%) followed by age group of 16 to 45 years (14.7%). Average axillary temperature was similar among both influenza positive and negative population. Majority (59.2%) tested positive for influenza virus, of which the most frequent was influenza A (59.9%). Conclusion: Influenza stands as an important public health threat. Surveillance of influenza helps in early warning system, to understand local outbreaks and to prepare for global pandemics. A larger study spanning over several years would have been more informative.

Keywords: Influenza, surveillance, pandemic, virus

INTRODUCTION

Influenza is usually a self-limited illness characterized by an abrupt onset of highfever, cough, sore throat, body aches, chills, headache, or fatigue lasting several days. Influenza can cause pneumonia, either viral or from bacterial super infection which may be lethal, particularly in the very young, very old, and chronically-ill patients.[1] The clinical presentation of influenza disease is indistinguishable from other respiratory viruses. Of the 3 types of influenza virus (A, B and C), types A and B are most often associated with disease outbreaks during the late autumn and early winter in temperate climates. In the tropics and subtropics (e.g. Nepal) influenza may occur throughout the year and/or with more intense activity during the rainy season.[2] Transmission of influenza virus is by person-to-person contact, airborne droplets, fomites and occasionally by pigs or birds.

Influenza infection results in a clinical syndrome not easily distinguished from other respiratory infections. Also, other viruses also circulate in what is often referred to as the influenza season. Other viruses that can cause clinical features similar to influenza are respiratory syncytial virus, adenovirus, parainfluenza virus, rhinovirus, human metapneumovirus among others. This has led to the use of the term 'influenza-like illness' to describe the clinical features that can be attributed to influenza and other respiratory viruses. According to WHO, using a common case definition globally allows health authorities across nations to interpret their data in an international context. WHO case definition for ILI is an acute respiratory infection with fever 38°C or more and cough, with onset within the last 10 days. [3-5]

Antigenic drift or antigenic shift of influenza virus produces new strains. The most devastating impact of influenza in the twentieth century occurred in 1918-1919 A.D when one quarter of the world's population was infected resulting in 20 million deaths. This pandemic was distinctive because of the larger number of fatalities among young adults. There have been three other pandemics, though less devastating, during the 20th century.[6-7]

The viral surface of influenza types A and B has two strain-specific molecules, hemagglutinin (H) and neuraminidase (N). Hemagglutinin allows the virus to attach to cells and neuraminidase allows the virus to spread from cell to cell. Four subtypes of H (H1, H2, H3 and in 1997 H5) and two subtypes of N (N1 and N2) have been recognized as causing human disease. Infection with a virus of one subtype provides little protection against viruses of other subtypes. An antigenic shift, which occurs at undefined time intervals, refers to a change from one H or N subtype to another and has the potential to cause pandemics. In pandemics, the population is not immune to the new subtype. An antigenic drift results from minor alternations in H or N antigens without a change in subtype. Epidemics due to antigenic drifts occur every one to three years. Recent vaccines have included two A-type and one B-type strains and a protective immune response develops in about two weeks but wanes over a year. [6-9]

The highly pathogenic avian influenza A (H5N1) epizootic (animal outbreak) in Asia, Europe, the Near East, and Africa is not expected to diminish significantly in the short term. It is likely that H5N1 virus infections among domestic poultry have become endemic in certain areas and that sporadic human infections resulting from direct contact with infected poultry and/or wild birds will continue to occur. So far,the spread of H5N1 virus from person-to-person has been very rare, limited and unsustained. However,this epizootic continues to pose an important public health threat. This strain poses a considerable human public health risk. Not only can these viruses infect humans, causing severe disease with high mortality, but there is also potential for them to adapt, or recombine with other influenza viruses, and give rise to a pandemic viral strain. [8-12]

For close global monitoring of the situation and co-ordination of the global response, WHO recommends enhanced surveillance for influenza A/H5. Surveillance of influenza locally and globally is an important effort that helps in early warning system, to understand, mitigate local outbreaks and to prepare for global pandemics.[3] Several outbreaks of influenza have been reported from many parts of Nepal in the past. The present study was performed at Pokhara Academy of Health Sciences(PAHS), Western Regional Hospital(WRH), Pokhara. Pokhara is a tourist hub of Nepal. WRH is a regional referral hospital for multi-disciplinary treatment. WRH is uniquely situated for surveillance since the local people, working in tourism and hospitality

sector are widely exposed to travellers from different part of the world. WRH is one of the sentinel sites for human surveillance of influenza in Nepal that is maintained by Walter Reed/ AFRIMS Research Unit Nepal (WARUN). WARUN also maintains other sentinel sites in Nepal and actively provides human influenza surveillance report to National Influenza Surveillance Network -National Influenza Center (NISN-NIC), Nepal which aids in global influenza surveillance and annual vaccine formulation against seasonal influenza.

In this study, ILI cases were studied in the following aspects : symptoms, demographics, seasonality and laboratory results.

MATERIALS AND METHODS

This is a retrospective study of surveillance report of tests of ILI carried out at PAHS, WRH. Firstly, approval for research was obtained from National Health Research Council, Kathmandu. Data from the time period July 1st 2018 to December 31st 2019 was taken. Symptoms of all patients were noted according to symptom score format. Demographic profiles were noted. Finally, laboratory test was performed and test report collected.

Enrollment

Patients presenting at WRH with influenza like illness (cough, sore throat and history of fever) were questioned for willingness to participate in the study. A written consent and/ or parental consent was obtained. Any patient, male or female of age 6 months or above with influenza like illness were eligible to enroll in the research.

Laboratory procedure

Two nasal swabs and one throat swab was collected from each subject. In each case, one nasal swab was used at the site lab(WRH lab) for rapid diagnostic test (RDT) for influenza A and B (Quidel QuickVue influenza a+b). The result of the RDT was provided free of cost to patient advising for prompt follow up with treating clinician. Remaining nasal swab and one throat swab were preserved in universal transfer medium (UTM) and kept in cold chain. The preserved samples (UTM) were transferred to WARUN in cold chain via domestic commercial air route. At WARUN, samples were tested for influenza by real-time reverse transcriptase polymerase chain reaction (rRT-PCR) assay.The probes and primers used in rRT-PCR were Universal Influenza Type B, Influenza Type A: Hemagglutinin H1, H1_pdm09, H3, H5, H7 & H9.

RESULTS

1213 cases were studied in the 18 months study period.

Demographics

Among 1213 subjects enrolled during study period, 63% were males. Mean age and standard deviation among male and female patients were comparable in both aggregate and specific age group. Proportions of males were notably higher among younger age group (< 15 years). Most patients are in the age group <15 years (82.5%) followed by the most economically active age group of 16 to 45 years (14.7%) (Table 1). Most of the participants were residents of Kaski (93.4%), followed by Tanahun (3.2%), Syangja and Parbat district(not shown in table).

Table 1: Demographics

Age Group	Values	Female	Male	Total
< 5 years	N (%)	239	441	680 (56.1)
	Mean age (years)	2.65	2.66	2.66
	Std. Dev	1.12	1.21	1.18
5 to 15 years	N (%)	111	210	321 (26.5)
	Mean age (years)	7.94	8.38	8.23
	Std. Dev	2.68	3.07	2.94
16 to 45 years	N (%)	85	93	178 (14.7)
	Mean age (years)	29.21	28.46	28.82
	Std. Dev	7.11	8.59	7.91
46 to 60 years	N (%)	11	18	29 (2.4)
	Mean age (years)	53.02	52.63	52.77
	Std. Dev	4.77	4.73	4.66
> 60 years	N (%)	2	3	5 (0.4)
	Mean age (years)	67.78	67.15	67.41
	Std. Dev	8.24	5.99	5.92
Total	N (%)	448 (36.9)	765 (63.1)	1213 (100)
	Mean age (years)	10.53	8.80	9.44
	Std. Dev	13.15	11.85	12.37

Laboratory results

All samples were tested by rRT-PCR for influenza, in which majority (59.2%) were positive for influenza virus. Among positive, majority were influenza A (59.9%)(Figure 1). Influenza was prevalent throughout the surveillance period (July 2018-December 2019). There were two distinct peak seasons observed, one during post rainy season and the other during late winter. Flu A/ H3 and Flu A/ H1_pdm09 dominated the peak seasons in turn. Flu B also co circulated with Flu A throughout the season and observed in high numbers during post rainy season of 2019 (Figure 2).

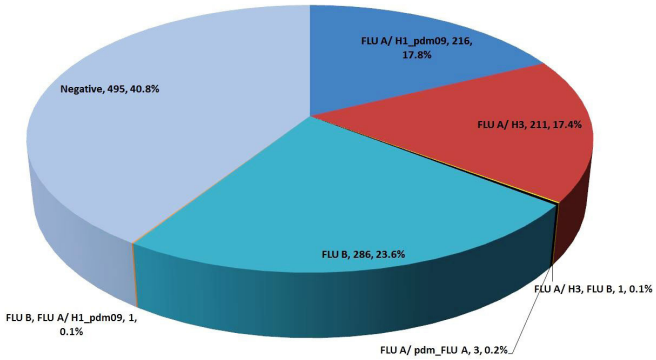

Figure1: Influenza confirmed by rRT-PCR among ILI cases

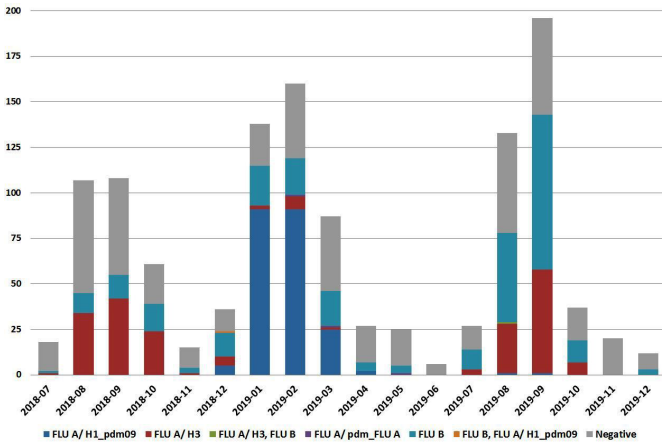

Figure 2: Seasonality of Influenza

Clinical features

Average axillary temperature was similar among both influenza positive and negative population, while symptoms score among the same groups was comparable with slightly high among positive group (Figure 3).

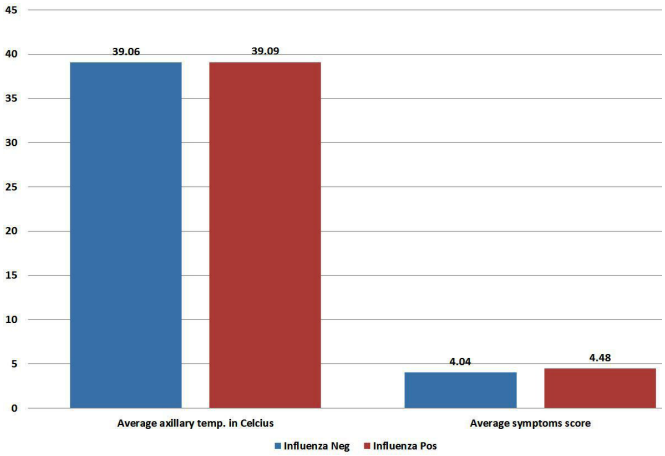

Figure 3: Clinical features

DISCUSSION

A prospective study across two influenza seasons in Taiwan showed that fever, cough, rhinorrhea, sneezing, and nasal congestion were significant predictors for influenza infection. The combination of fever plus cough had the best sensitivity (86%), but the combination of fever plus cough and sneezing had the best specificity (77%).[13] In the present study, cases were screened according to WHO case surveillance definition for ILI.

A definitive set of symptoms for a clinical diagnosis of influenza has been difficult to achieve. All surveillance definitions of influenza include cough and fever.[4] The Australian Sentinel Practice Research Network (ASPREN) definition of influenza is more complicated and relies on the recognition of influenza circulating in the community combined with a number of respiratory and systemic symptoms. Influenza case definition includes fever with chills/rigor , cough, weakness, myalgia among others. [4]

In another study, authors concluded that ILI criteria were poorly related to laboratory-confirmed influenza.[14] They advised that a less restrictive clinical criterion (specifically, acute respiratory infection) should be applied for early detection of influenza viruses in surveillance systems. In their study, throat specimens were collected from outpatients with acute respiratory infection (≤72 hours duration). Laboratory-confirmed influenza infection was compared with independent symptoms and the influenza-like illness criteria,

as defined by the Classification Committee of the World Organization of Family Doctors. From 1934 patients, 359 (18.56%) yielded positive results for influenza viruses. Only 199 (55.4%) of laboratory-confirmed cases fulfilled clinical criteria of ILI. Over four years of active sentinel surveillance caonducted in Bali, Indonesia, between 2010 and 2014, determined that 22% of ILI cases were associated with laboratory confirmed influenza infection, with year-round influenza virus circulation on the island and higher influenza activity during the wet season.[15]In our study, throat and nasal swabs were collected from patients with ILI features (upto 3 days for outpatients and upto 5 days for inpatients from symptom onset). 59.2 % of subjects tested positive for influenza. In our study, majority of patients tested positive for influenza. This may be because of specific criteria adopted for ILI cases and also because the study samples were collected during early infection stage when there is higher chances of viral shedding.

Ten year surveillance data was published by Nisar N et al. Influenza A/H1N1pdm09 was the predominant strain with 40.6% (n=1442) followed by influenza B (936, 26.4%).[16] Influenza A/ H1N1pdm09 was predominant among the children (5-14 years) and adults (15-64 years). Influenza B strain was predominantly found in the elderly age group (≥65 years) which is 48% of cases followed by children (2-4 years) accounting for 37% of cases. It was inferred that influenza activity in their country occurred throughout the year with seasonal winter peaks. Surveillance in our study showed that Flu A/ H3 and Flu A/ H1_pdm09 dominated the peak seasons in turn. Flu B also co -circulated with Flu A throughout the season and observed in high numbers during post rainy season.

CONCLUSION

Majority (59.2%) of studied cases tested positive for influenza virus, among which, influenza A (59.9%) was the predominant infection. Influenza was prevalent throughout the surveillance period. Surveillance of influenza helps in early warning system, to understand local outbreaks and to prepare for global pandemics. A larger study over a longer period of time(several years) covering a much larger number of cases would be more informative to understand the epidemiology and disease spectrum regarding influenza infection in our city, Pokhara.

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